TETANUS.

BY CHARLES M. BLACKFORD, JR., M. D.,

OF LYNCHBURG, VIRGINIA.

REPRINTED FROM TRANSACTIONS OF MEDICAL SOCIETY OF VIRGINIA, 1892.

TETANUS.

The Essay for which Dr. Hunter McGuire's Prize of One Hundred Dollars was Awarded.

Signed "Non Sine Semine."

By CHARLES M. BLACKFORD, Jr., M. D., of Lynchburg, Va.

Tetanus may be *defined* as an acute, infectious disease, characterized by tonic contractions of the muscles, or groups of muscles, usually commencing with the muscles of mastication.

As a preliminary to the study of the pathology of tetanus, it will be of value to review the *conditions under which muscular tissue normally contracts, and the phenomena attending its contraction.*

In common with all the specialized tissues, a stimulus is required for it to exhibit its peculiar function, and this stimulus may be applied either to the motor nervous mechanism, or directly to the muscle, for the presence of nerve-fibres seems not to be essential for the response to stimuli on the part of the muscle. If a blow be struck the tendon of the gastrocnemius of the frog, in which, as yet, no nerve-fibres have been detected, a wave of contraction follows in the muscle, which is thought to be due to the direct irritation of the sarcous material by the blow. Another reason for thinking that muscular tissue possesses inherently the power of contracting, independently of nervous influence, is that certain substances applied to the muscle produce contraction, whereas, when applied to the nerve, the result is negative. Thus, mineral acids, oxalic and acetic acids (Kühne), the salts of iron, zinc, copper, silver, and lead, and,

in addition to these, bile also (Budge), *act in very weak solutions as muscular stimuli*, while they act on the motor nerves only when concentrated. Gases and vapors generally act as muscular stimuli, but the vapor of carbon bi-sulphide acts only as a nervous stimulus. (Kühne and Jani.)

In addition to these chemical stimuli, a gradually raised temperature excites contraction—this beginning when the temperature reaches about 30° C. and attaining a maximum at about 45° C. (Eckard.) Should the temperature continue to rise, the muscle will pass into the "heat rigor." As before mentioned, a blow will cause contraction, as also will a current of electricity.

The normal stimulus, however, reaches the muscle through its motor nerve. The motor impulse in voluntary movement originates in a motor centre in the cerebral cortex, passes through the corona radiata, the internal capsule, through the decussation of the motor fibres in the medulla, and is transmitted by the direct and crossed lateral tracts in the cord to the anterior roots of the spinal nerves, and thence to the muscle. It will be seen that a chemical, thermal, mechanical, or electrical stimulus may be applied anywhere throughout this long chain, and will be followed by a response on the part of the muscle.

There is one other mechanism to be considered—that of the so-called reflex movements. The arrangement of a reflex is simple, consisting only of an afferent nerve, conveying impressions to the "centre;" the "reflex centre," which receives the impression brought it by the afferent nerve, and responds to it by sending an impulse over the third element—the efferent nerve, which conducts the impulse from the centre to the muscles connected with the particular reflex. It is evident that, to produce a reflex movement, a stimulus can be applied either in the course of the afferent nerve or to the centre itself. Ordinarily, in reflex actions, a stimulus is applied to the terminus of the afferent nerve, by which it is transmitted to the centre. The centre then acts more or less violently, sending impulses over the efferent nerve to the muscles involved. Some reflex centres seem to be normally acted upon directly, and not through an afferent nerve, though they are capable of the usual indirect excitation. An instance of this is the respiratory centre, whose

usual stimulus is an excessive amount of carbon dioxide in the blood, though it can be excited by dashing cold water on the breast of the subject. The response varies somewhat in proportion to the vigor of the stimulus, and the general excitability of the centres may be increased or diminished by various agencies that will be considered further on in this paper.

A stimulus being applied to a muscle under proper conditions, the muscle contracts. It becomes shorter, thicker, and firmer. It loses a little in bulk, its specific gravity is slightly raised, it becomes, strange to say, more elastic; the amount of oxygen consumed, and of carbon dioxide given off by it, are increased, though these are not in a constant ratio. The extractives soluble in alcohol increase, and those soluble in water diminish. Sarco-lactic acid, and a peculiar muscle-sugar called inosite, make their appearance. The temperature rises, and the normal electrical current is stopped or reversed.

But an analysis of the process of contraction, made with the myograph, is even more instructive. We find that after stimulation there is a latent period during which the muscle apparently is unchanged; then contraction commences, goes on to its maximum, and subsides. This contraction commences at the point of stimulation, and moves in a wave-like manner through the muscle in every direction at a rate that varies in different animals and in different muscles of the same animal. In the arm-muscles of man, the rate of progression is from four to five metres per second. (Power.)

Now, this cycle of phenomena requires time for its performance, and a second stimulus may be applied before the effect of the first is lost. If this be applied at the end of the first latent period, it will be seen that after attaining the maximum contraction for one stimulus, the muscle will contract still more as a response to the second; and if these stimuli be repeated at short intervals—too short for relaxation to occur—the muscle will be thrown into a state of *tetanus*, in which the curve of the myogram becomes practically a straight line, showing that, for all intents and purposes, there is no relaxation. But, strictly, this is not true, for a tetanic muscle emits a clear musical note that is due to its rapid vibration, though these vibrations, while it is in this

condition, have so slight an extent, and are so rapid, that we have no means of recording them.

It thus appears that the condition known as tetanus may be produced under perfectly normal circumstances, by rapidly-repeated stimuli, applied without allowing time for relaxation. Many observers think that the ordinary contraction following an impulse of the will is really the physiological tetanic condition.

In treating of the *pathological condition* that is called tetanus, I propose to reverse the usual order in which the subdivisions of the subject are considered, and to take up the *symptoms, especially their similarity to strychnia poisoning*, before discussing the pathology and etiology. This arrangement seems logical, as it is a statement of the premises on which the causation of the disease rests as a conclusion.

Tetanus is usually divided into two classes—*traumatic* and *idiopathic*—to which some pathologists add *trismus nascentium*, though others, among whom is the writer, prefer to class this under the first division. The symptoms of traumatic tetanus are, unfortunately, but too familiar to the medical profession. It may be well, however, to give a summary of them here.

At a varying time after the receipt of the injury, which may be merely an abrasion of the skin, the patient complains of "soreness in the throat." On examination of the wound, it will be seen to look unhealthy, more or less inflamed, and suppurating slightly or profusely. The discomfort in the throat is rapidly followed by constriction in the pharynx, rigid contraction of the masseter muscles, dysphagia, and dyspnœa. The skeletal muscles are next involved, giving rise either to a lateral bending of the body (pleurosthotonos), or a backward bending (opisthotonos). The mouth is sometimes drawn outward, and the eyebrows elevated, giving a sort of grin, called the risus sardonicus. As a rule, no rise of temperature occurs at the beginning of the attack, and may not occur throughout it, though sometimes it rises even as high as 112° F. before death. The reflex excitability is greatly increased, clonic spasms being brought on by dressing the wound, or even a draught of air striking the patient. The intellect is clear to the end, or at least until carbonic oxide poisoning ensues from tonic contraction of the respiratory muscles.

In addition to those enumerated above, there are other symptoms that may be present. Among them are profuse perspiration, obstinate constipation, scanty and high-colored urine, possibly delirium, though this is thought to be due generally, if not invariably, to the drugs used to allay the spasm. (J. Hutchinson, Jr.)

The striking similarity of these symptoms to those of strychnia poisoning cannot fail to impress itself on the observant mind. That this similarity may be clearly shown, a review of the chief phenomena of the latter will be given. After taking a lethal dose of strychnia, or one of its salts, an interval of varying length occurs, which corresponds to the latent period in tetanus. This being past, the patient complains of restlessness, uneasiness, and a sense of impending suffocation, attended by a shuddering or twitching of the muscles. The tetanic convulsions then commence suddenly and violently, involving the muscles of mastication, though usually they are among the last to be affected. Frequently, the patient can speak and swallow during a paroxysm, a condition which rarely or never obtains in pathological tetanus. Excessive thirst is frequently a prominent symptom, thereby marking another point of difference between the two conditions.

But the most characteristic feature of strychnia poisoning is the remission that succeeds the spasm. The patient lies rigid, or in a state of opisthotonos for a time, and then the convulsion passes off, leaving the patient much exhausted and bathed in perspiration. A very slight stimulus will again bring on an attack, showing that there is a hyperæsthetic condition of the reflex centres. The life of the patient, after the tetanic spasms commence, may, as a rule, be counted in minutes, whereas, in true pathological tetanus, life may be prolonged for twenty-four hours or more. This will be explained later.

It is apparent, from this comparison of symptoms, that it is not unlikely that the disease is the result of toxic doses of some agent whose physiological action is like that of strychnia. If this be demonstrated, it will be easy to prevent the disease by preventing the access of the poison, as it is easy to prevent strychnia poisoning by abstaining from the drug.

We will next consider the *post-mortem lesions found in the two conditions* that we have been comparing. These are of little value for diagnostic purposes, but will be used later to demonstrate the etiology.

In *strychnia poisoning, the lesions* are of a variable character, the most constant feature being a marked congestion of the medulla and spinal cord. Now, it is a well-known physiological fact that functional activity occasions an afflux of blood to a part; and as the reflex centres, that are in a state of over-activity, are situated in the cord and medulla, it is more than probable that the hyperæmia is due to the exalted activity of these centres, and is not its cause. According to Spitzka, as quoted by Bartholow (*Mat. Med. and Ther.*), chronic poisoning by strychnia causes disease in the cord, "partly as an insular sclerosis, partly as a hæmorrhagic or non-hæmorrhagic myelitis." In brief, strychnia produces no lesions due exclusively to the drug. The ecchymoses found in the viscera, and the extravasations of blood in the muscles, can readily be explained by the violence of the convulsions.

In tetanus, *microscopical examination* yields yet more scant results. Frequently, nothing abnormal is found, though at times minute hæmorrhages, or even extensive extravasations of blood or serum, can be seen. Other observers report granular degeneration, centres of softening, nuclear proliferation with the formation of fat granules or amyloid bodies. In other words, they report evidence of rapid and extensive tissue changes; but, as Dercum puts it, "they are, so to speak, the marks of devastation left by the storm."

Summing up this testimony, we find that there are no lesions indicating any specific disease of the nervous system, though the symptoms indicate excessive activity on the part of that system. The disease seems to be a hyperæsthetic condition of the reflex centres, similar to that caused by strychnia.

With this hypothetical pathology in view, let us analyze the symptoms more thoroughly than we have yet done. The patient complains of restlessness and uneasiness in both conditions. In tetanus, there is a spasm of the muscles of the throat; in strychnia poisoning, there is a feeling of constriction of the

throat, which seems to indicate the same pathological condition, though differing in degree. In both the temperature rises, but, as has been shown, it is normal for the temperature to rise when muscular action is excited. There is sometimes a profuse perspiration, but this is also attendant on active muscular exertion. In both, the mental faculties are unaffected, showing that the higher centres are unaffected by the toxic agent. In both death comes from exhaustion or carbon dioxide poisoning.

That there are agents that exalt the reflex excitability of the spinal centres, is undoubted. Ignatia and quebracho are used therapeutically for this very purpose, and it is not at all impossible, or even improbable, that tetanus may be merely the physiological effect of an agent having similar action.

This brings us to the consideration of the *cause of tetanus*. To within the last few years this has been a *terra incognita* to surgeons, and has proved no exception to the rule that the unknown is terrible. Even so late a writer as Gibson says (*Institutes and Practice of Surgery*, Vol. II, page 474), after stating the old view that it was due to the wounding of a nerve, "On the other hand, it must be confessed that dissection has been frequently unable to reveal to us the source of this inexplicable and most formidable malady."

The fact that the occurrence or non-occurrence of tetanus after an injury bore no relation to the site or extent of the injury, was an obstacle that the earlier pathologists found difficulty in surmounting, but at length it has been overcome, and the etiology of this serious disease is being cleared up.

In 1884, Nicolaier* observed that the inoculation of mice, guinea-pigs, and rabbits, with small particles of earth, would almost invariably produce tetanus, though, if the earth were previously heated to a temperature of 150° C., this result would not follow. Further investigations made by means of "cultures," were productive of a bacillus which he thought to be the specific cause, though he was unable to isolate it. Rosenbach† found this bacillus in the pus from a case of tetanus, and by experiment confirmed the claims of Nicolaier. Senn‡ has given at length

* *Deutsche Med. Wochenschrift*, No. 52, 1884.
† *Langenbeck's Archiv.*, B. XXXIV, p. 306.
‡ *Surgical Bacteriology*, by N. Senn, M. D., pp 144–152.

the confirmatory experiments made by many investigators, so that it is unnecessary to repeat them here; but suffice it to say that the concensus of opinion among those qualified to judge is that the disease is caused by a specific bacterium which has received the name of the *bacillus tetanus.**

But how does this minute organism produce this result? The answer is not far to seek. It is well known that certain by-products result as an incident to the metabolism of all kinds of organisms. Thus urea, and the almost innumerable products found in the intestinal canal, are by-products resulting from the life of the human organism; morphine is a result of the life-work of the poppy; and, to render the parallel still more striking, strychnia is a product of the cell-life of the nux vomica. Similarly, the minute plant, called the bacillus tetanus, finding a soil suited to it in the unprotected wound, grows, and as the result of its life, the alkaloid *tetanine* is produced, the action of which is similar to strychnia. The slower action of tetanine is due to its being more slowly absorbed, for it can be absorbed only so fast as it is formed, and it is of slow formation.

That I may be more readily understood, I wish to give here a brief account of the *methods by which bacterial studies are pursued*, and show the scrupulous care necessary to obtain results that can be relied upon as accurate and of scientific value.

I will begin by describing the nutritive media in which micro-organisms are cultivated. These media differ somewhat from the different organisms. The one most used is a gelatinized beef broth. This is prepared by macerating two pounds of lean beef in one litre of distilled water at a temperature of about 35° C., until all the nutriment is extracted, skimming off the fat, straining, and then boiling the clear fluid for about an hour to kill any micro-organisms that might be in it. A test-tube or flask must then be "sterilized." This is accomplished by washing in a 1:1000 solution of corrosive sublimate, then in boiled water, and by finally placing it in a steam sterilizer for about two hours. It should now be plugged with clean cotton, and heated to about 200° C. to sterilize the cotton. A higher temperature is required for the dry heat than for steam, because, when

* See further Lamiasi in *London Lancet*, April 27, 1890.

bacteria are dried and exposed to heat, their vitality is frequently but suspended, and activity is resumed when moisture again reaches them.

The sterilized test-tube should now be filled about two-thirds full of the sterilized nutrient broth, to which about five per cent. gelatine, also sterilized, should be added. Replace the cotton plug as quickly as possible, and place the whole in a steam sterilizer for some hours, to kill any spores that may have gained admittance during the time of exposure. Now, let the culture soil stand in a warm place for a day or so, and if no micro-organisms develop, it will then be ready for use.

Many experimenters, among whom is the writer, prefer sterilized blood-serum for the medium in making cultures of tetanus; indeed, some claim that nothing else will do. The general mode of preparation is similar to that of the gelatine soil, but more care is necessary to prevent the serum from becoming opaque at the temperature requisite for sterilization.

Supposing that the medium is ready, the next step is to inoculate it with the bacilli. A platinum needle is heated to a white heat in an alcohol flame, and as soon as it has cooled, is dipped in the pus from which the cultures are to be made, and the culture-tube impregnated. The cotton-plug is withdrawn while the tube is held in an inverted position, and a deep stab made in the gelatine. The cotton is replaced, and the tube restored to an upright position. It is now important that the tube be not exposed to extremes of temperature; indeed, the more uniform the temperature the better.

Should all go well, in about twenty-four hours there will be a faint cloud floating in the gelatine. This is the "mixed culture," for in addition to the specific bacterium of tetanus, there will be found some of the ordinary pus-forming bacteria, especially the staphylococcus pyogens albus or aureus. These liquefy the gelatine, and cause a granular precipitate at the bottom of the tube, which is either gray or orange, according to the species present; but some bubble-like appearances will also be seen in the gelatine. These are the colonies of the bacilli of tetanus.

It is very difficult to get a pure culture, as the other genera cling very persistently to the tetanus, but it can be done.

Kitasato* obtained it by innoculating a rat at the root of its tail with the mixed culture, and after its death from tetanus a culture was made from the wound. By repeating this process, from tube to animal, and from animal to tube, a pure culture can at last be gotten. When isolated, it is seen to be a slender rod, bearing a spore on one end which gives it somewhat the appearance of a minute pin.

Now, in the course of the lives of these micro-organisms, there is produced a substance that presents many analogies to the alkaloids, and which, following the nomenclature used for the alkaloids, has been called *tetanine*. Since tetanine was isolated, Brieger† has obtained three other toxic materials from these cultures, and has described, with great fullness, their physiological action. I condense his account of the four substances. The first, *tetanine*, in a dose of a few milligrams, produced in mice the characteristic symptoms of tetanus. The second, *tetatoxine*, produced tremors at first, and later convulsions and paralysis. The third, which was *not named*, produced well-marked tetanic symptoms, and also excited the salivary and lachrymal glands to increased activity. And the fourth, *spasmotoxine*, produced tonic and clonic spasms, which at once prostrated the animal. It is thus seen that the symptoms of tetanus may all be explained by the physiological action of these ptomaines.

The reader has doubtless noticed that nothing has been said about "idiopathic" tetanus, nor infantile tetanus. The reason for this is that although, in deference to the standard writers, the older classification is nominally and clinically observed, pathological writers of to-day are inclined to regard all tetanus as traumatic. The size and nature of the wound is of no consequence—the scratch of a pin, the prick of a needle, being enough to furnish a nidus for the growth of the specific agent; and to claim that so trifling a wound could not be the starting point of the disease is like claiming that strychnia poisoning could not be produced by hypodermic injection because of the minute size of the puncture. The wound is only the avenue through

---

* *Zeitschrift für Hygiene*, Bd. VII, p. 225.

† Zur Kenntniss der Ætiologie des Wundstarrkrampfes nebst Bemerkungen über das Cholera-roth. *Deutch Med. Wochenschrift*, 1887, p. 303.

which the poison gains access to the body; and since the micro-organisms generate the poison, a microscopic wound would be sufficient for infection to take place. As every one constantly receives minute injuries, and pays no attention to them, the absence of a history of a wound is not conclusive proof that none has been received. In the case of infants, the umbilical wound is the usual point of infection.

We may now sum up the results of the investigations made in regard to tetanus somewhat in the form of a syllogism; and if so arranged, it falls into the following form:

1. Tetanus consists essentially of a tonic spasm of certain muscles or groups of muscles, which have been thrown into the state of physiological tetanus.

2. This is caused by an abnormal irritability of the reflex centres in the medulla and cord.

3. This hyperæsthesia is the result of the physiological action of certain ptomaines, or alkaloids of decomposition, formed in a wound and absorbed therefrom.

4. These ptomaines are the result of the growth of a specific bacterium called the bacillus of tetanus or the bacillus of Nicolaier, and only by it. Therefore,

5. Tetanus is a toxic disease, caused by the infection of a wound by this specific bacterium, or its products.

Let us, finally, consider *the treatment*. In this disease, almost above all others, is the cheap ounce of prevention preferable to the more costly and difficult pound of cure. As soon as the patient comes under observation, the wound must be thoroughly explored and cleaned. All foreign substances, especially bits of wood, street dust, straw, hay, pieces of clothing, and the like, must be removed with scrupulous care, and the innermost recesses of the wound opened and exposed to the action of a germicide. Iodoform or aristol should be freely used, not for their germicidal action, which is small if existent at all, but for their undoubted power of decomposing ptomaines, perhaps through the iodine they contain. Corrosive sublimate and carbolic acid remain our chief aids in rendering the wound surgically clean, and should be used first—the iodoform or aristol being used after disinfection.

I wish to emphasize in every way, that every instrument, ligature, bit of sponge or cotton—everything, in fact, that touches the wound, should be thoroughly disinfected. With scrupulous care, see that the wound is aseptic, and, as an additional precaution, with the use of antiseptics, tetanus will not occur; and if it does, it is a sure indication that the wound has been contaminated by some error of omission or commission on the part of the surgeon.

There is a prevalent idea that wounds of the hands and feet are peculiarly liable to be followed by tetanus, but this is only due to the fact that the feet and hands are particularly liable to become dirty, and are more difficult to cleanse.

Should the attack commence, the first indication is to stop the formation of the ptomaine. With this in view, the wound should be opened and disinfected, sometimes with the actual cautery. The writer thinks that strong (1:250 or 1:500) solutions of corrosive sublimate will do as well, and these last have the advantage of avoiding the shock incident to the use of the curette or cautery. The room should be absolutely quiet, to avoid peripheral irritation as much as possible. The bed-clothes should be light, and, if practicable, supported on a frame above the patient so as not to touch him. Potassium bromide or chloral is to be given in large doses by mouth or rectum, either together or separately. Chloroform and ether have but doubtful value, for, to produce any effect, they must be given to full anæsthesia; and as the patient has difficulty in breathing any way, it is unwise to throw a further obstacle before him. Amyl nitrite is recommended, but the writer has had no personal experience with it. Curara seems to be indicated, and some writers claim good results from its use. It is worthy of more extended trial in this and similar diseases. Opium in large doses will frequently be of service, and digitalis, ammonia or alcohol may be needed as stimulants.

Physostigma, however, is our chief reliance among drugs. A third of a grain of the extract subcutaneously, or a grain by the stomach, is enough to commence with, and the dose should be repeated in two hours. It is far more elegant to use than salicylate of physostigmine subcutaneously, and it has the additional

advantage of avoiding the pain and spasm that attends an attempt to swallow. Although comparatively few cases have as yet been reported, the success of this treatment is very gratifying.

Dr. R. Schwartz,* of Padua, announces the successful use of the "tetanus antitoxíne," discovered by Tizzoni and Caltani, for the prevention and cure of tetanus. By using this product hypodermically, immunity against the disease was produced, even in animals susceptible in a high degree; and it was shown that the blood serum of these immune animals exerts an antitoxic action, and is capable of producing immunity against, and cure of the disease. Tetanus antitoxine may be produced in a solid shape by adding alcohol to the serum of an inoculated animal, and evaporating *in vacuo*. As the disease in man is of longer duration than in many animals, it is to be hoped that the timely use of this agent may be of use. Schwartz relates the case of a boy of fifteen years of age treated by him, and says that Gagliardi, of Molinella, treated a severe case by hypodermic injection of one gramme with disappearance of all symptoms and complete recovery. It is hoped that further use may confirm these brilliant results.

* *New York Medical Record*, Vol. XLI, p. 126.